IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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10/8/98

In re Application of:

GEERT MAERTENS
LIEVEN STUYVER

Serial No.: 08/836,075

Filed: April 21, 1997

For: NEW SEQUENCES OF HEPATITIS C VIRUS GENOTYPES AND THEIR USE AS PROPHYLACTIC, THERAPEUTIC AND DIAGNOSTIC AGENTS

Group Art Unit: 1643

Examiner: M. Zeman

Attorney Docket: INNS004/KAM

AMENDMENT AND RESPONSE TO OFFICE ACTION DATED MARCH 23, 1998

CERTIFICATE OF MAILING
37 C.F.R 1.8

I hereby certify that this correspondence is being deposited with the U.S. Postal Service as First Class Mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231, on the date below:

September 23, 1998 Patricia A. Kammerer

Assistant Commissioner for Patents

Washington, D.C. 20231

Sir:

This paper is submitted in response to the Office Action dated March 23, 1998 for which the three-month date for response was June 23, 1998.

A request for a three-month extension of time to respond is included herewith along with the required fee. This three-month extension will bring the due date to September 23, 1998, which is within the six-month statutory period. Should such request or fee be deficient or absent, consider this paragraph such a request and authorization to withdraw the appropriate fee under 37

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C.F.R. §§ 1.16 to 1.21 from Arnold, White & Durkee Deposit Account No. 01-2508/INNS004/KAM.

Reconsideration of the application is respectfully requested.

I. AMENDMENT

Please make the following amendments:

IN THE CLAIMS:

63. (Amended) A Hepatitis C virus polynucleic acid, having a nucleotide sequence which is unique to at least one of the new HCV types 7, 9, 10 or 11, or, to at least one of the subtypes 1d, 1e, 1f, 1g, 2e, 2f, 2g, 2h, 2i, 2k, 2l, 3g, 4k, 4l or 4m, wherein when the sequence is unique to at least subtype 1d the sequence is at least 96% identical to SEQ ID NO: 1; or the complement thereof.

64. (Not amended) A polynucleic acid which is chosen from the group consisting of the nucleotide sequences having SEQ ID 1, 3, 5, 7, 9, 11, 13 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103 or 105, or the complement thereof.

65. (Amended) A polynucleic acid according to claim 63, wherein the polynucleic acid is selected from

(i) a polynucleic acid encoding an HCV polyprotein comprising in its amino acid sequence at least one of the following amino acid residues; I15, C38, V44, A49, Q43, P49, Q55, A58, S60 or D60, E68 or V68, H70, A71 or Q71 or N71, D72, H81, H101, D106, S110, L130,

I134, E135, L140, S148, T150 or E150, Q153, F155, D157, G160, E165, I169, F181, L186, T190, T192 or I192 or H192, I193, A195, S196, R197 or N197 or K197, Q199 or D199 or H199 or N199, F200 or T200, A208, I213, M216 or S216, N217 or S217 or G217 or K217, T218, I219, A222, Y223, I230, W231 or L231, S232 or H232 or A232, Q233, E235 or L235, F236 or 6236, F237, L240 or M240, A242, N244, N249, I250 or K250 or R250, A252 or C252, A254, I255 or V255, D256 or M256, E257, E260 or K260, R261, V268, S272 or R272, I285, G290 or F290, A291, A293 or L293 or W293, T294 or A294, S295 or H295, K296 or 3296, Y297 or M297, I299 or Y299, I300, S301, P316, S2646, A2648, G2649, A2650, V2652, Q2653, H2656 or L2656, F2659, K2663 or 12663, A2667 or V1667, D2677, L2681, M2686 or Q2686 or E2686, A2692 or K2692, H2697, I2707, L2708 or Y2708, A2709, A2719 or M2719, F2727, T2728 or D2728, E2729, F2730 or 72730, I2745, V2746 or E2746 or L2746 or K2746, A2748, S2749 or P2749, R2750, E2751, D2752 or N2752 or S2752 or T2752 or V2752 or I2752 or Q2752, S2753 or D2753 or G2753, D2754, A2755, L2756 or Q2756, R2757, with said notation being composed of a letter representing the amino acid residue by its one-letter code, and a number representing the amino acid numbering as shown in Table 1,

(ii) [or] a part of said polynucleic acid of (i) which is unique to at least one of the HCV subtypes or types as defined in claim 63, [and which contains at least one nucleotide differing from previously known HCV nucleotide sequences,]

(iii) or the complement [thereof] of the polynucleic acid of (i) or (ii).

66. (Amended) A [polynucleotide] polynucleic acid according to claims 63 [to] or 65, wherein the polynucleic acid is selected from

(i) [with said] a polynucleic acid encoding an HCV polyprotein comprising in its amino acid sequences at least one amino acid sequence chosen from the group consisting of the amino acid sequences having SEQ ID 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104 or 106,

(ii) [or] a part of said polynucleic acid of (i) which is unique to at least one of the HCV subtypes or types as defined in [claims] claim ~~63~~ 1 [and 64, and which contains at least one nucleotide differing from known HCV nucleotide sequences],

(iii) or the complement [thereof] of the polynucleic acid of (i) or (ii).

67. (Amended) A polynucleic acid according to any of claims ~~63~~ 1 [to] or ~~65~~ 3, wherein the polynucleic acid is selected from [with said]

(i) a polynucleic acid encoding an HCV polyprotein comprising in its amino acid sequence at least one amino acid sequence chosen from the group consisting of the amino acid sequences having SEQ ID 107 to 207,

(ii) [or] a part of said polynucleic acid of (i) which is unique to at least one of the HCV subtypes or types as defined in [claims] claim ~~63~~ 1 [and 64, and which contains at least one nucleotide differing from previously known HCV nucleotide sequences],

(iii) or the complement [thereof] of the polynucleic acid of (ii) or (iii).

~~68~~. 16. (Amended) A polynucleic acid according to any of claims ~~63~~ 1 to ~~67~~ 55 which [codes for the] comprises 5' UR sequences, the Core/E1 and the NS4 or the NS5B region or a part thereof.

69. (Amended) A recombinant polypeptide encoded by a polynucleic acid according to any of claims 63 to 68, or a part thereof which is unique to at least one of the HCV subtypes or types as defined in claims 63 and 64[, and which contains at least one amino acid differing from previously known HCV types or subtypes amino acid sequences, or an analog thereof being homologous and biologically equivalent to said polypeptide].

70. (Amended) A method for production of a recombinant polypeptide of claim 69, comprising:

transformation of an appropriate cellular host with a recombinant vector, in which a polynucleic acid or a part thereof according to any of claims 63 to 68 has been inserted under the control of the appropriate regulatory elements, the polynucleic acid or the part thereof thus being an insert,

culturing said transformed cellular host under conditions enabling the expression of said insert, and

harvesting said polypeptide.

71. (Not amended) A recombinant expression vector comprising a polynucleic acid or a part thereof according to any of claims 63 to 68 operably linked to prokaryotic, eukaryotic or viral transcription and translation control elements.

72. (Not amended) A host cell transformed with a recombinant vector according to claim 71.

73. (Amended) A peptide corresponding to an amino acid sequence encoded by at least one of the polynucleic acids according to any of claims 63 to 68, with said peptide comprising an epitope which is unique to at least one of the HCV subtypes or types as defined in claims 63 and 64[, and with said peptide containing at least one amino acid differing from any previously known HCV type or subtype amino acid sequences, or an analog thereof being homologous and biologically equivalent].

Please add new claim 74:

--74. The polynucleic acid of claim 63, wherein when the sequence is unique to at least subtype 1d the sequence is at least 99% identical to SEQ ID NO:1.--

II. RESPONSE TO OFFICE ACTION

Support for the amendment of claim 63 and new claim 74 is given in the specification at p. 10, line 26 to p. 11, line 2. The amendments of claims 65-70 and 73 are intended to clarify the language of the claims and are supported by the claims as originally filed.

The points raised by the Examiner in the Detailed Action will be addressed in the order given.

Point 4 is related to a rejection of claims 65-73 under 35 U.S.C. §112, second paragraph, as being indefinite. (The rejection of claims 71-72 is based on the dependence of these claims on other, rejected claims). Specific aspects of this rejection, and how the amended claims are believed to overcome this rejection, are discussed below.

Claim 65 is rejected because the claim is understood by the Examiner to be directed to a complement of SEQ ID NO:1 which encodes the amino acid residues listed in claim 65. The

claim has been amended to clarify that it is directed to either (i) an HCV polynucleic acid encoding at least one of the listed amino acids, or (ii) an HCV polynucleic acid consisting of a portion of (i), or (iii) an HCV polynucleic acid consisting of the complement of (i) or (ii). The claim is not to be interpreted as requiring a listed amino acid to be encoded by (iii).

In claims 65-67, 69, and 73, the limitation requiring "at least one nucleotide differing from previously known HCV nucleotide sequences" is deemed unclear. This phrase has been deleted.

Claim 66 recites a "polynucleotide acid." A polynucleic acid was intended, and the appropriate amendment has been made.

Claims 66-67 depend from any one of claims 63-65, but their dependence from claim 64 is deemed improper. The claims have been amended to remove the improper dependence.

Claim 68 contains the phrase "which codes for the 5'UR" which is deemed indefinite. The Examiner proposed "which comprises 5' UR sequences" as being definite. The Examiner's proposed amendment has been incorporated.

Claims 69 and 73 contain the expression "homologous and biologically equivalent" which is deemed unclear. The phrase containing this language has been deleted.

Finally regarding point 4, claim 70 was found to lack antecedent basis for the phrase "said insert." "Insert" is now recited to provide antecedent basis.

Point 6 of the Detailed Action addresses a rejection of claims 63, 65-69, and 73 under 35 U.S.C. §102(b) as being anticipated by Qu et al. Specifically, Qu et al. report an HCV sequence with 91-95% identity to SEQ ID NO:1, which HCV sequence may be defined as being of subtype 1d. This rejection is believed to be overcome by amended claim 63, which requires

HCV polynucleic acids of subtype 1d to further have at least 96% identity with SEQ ID NO:1. New claim 74 raises the identity requirement to 99%. As the Examiner has pointed out, Qu et al. report a sequence with only 91%-95% identity with SEQ ID NO:1, which is below the identity requirements recited in claims 63 and 74. Therefore, the rejection is overcome.

Point 7 relates to a rejection of claims 63, 65-69, and 73 under 35 U.S.C. §102(a) as being anticipated by Okamoto, JP 06-319563. It appears this rejection is improper based on the priority date of the present application, 21 October 1994, as discussed above. JP 06-319563 is dated 22 November 1994. Therefore, it is believed the rejection should be withdrawn.

Point 9 relates to a rejection of claim 64 under 35 U.S.C. §103(a) as being unpatentable over Qu et al. or Okamoto, in view of the state of the art. Specifically, it is deemed obvious to screen HCV positive donors for other sequences of HCV subtype 1d.

Okamoto may not be the basis for such a rejection for the reasons given in response to point 7 above. Regarding the rejection over Qu et al., Applicants respectfully traverse. Accepting, for the sake of argument only, that it would be obvious to one skilled in the art to try to screen HCV positive donors for other HCV 1d sequences, it cannot be considered obvious that one skilled in the art would succeed in finding an HCV 1d sequence comprising a sequence identified in claim 64, e.g. SEQ ID NO:1. At the time of the invention, variation of HCV subtypes across geographic and ethnic distributions of hosts was unpredictable (see, e.g., the specification at Examples, pp. 50-56). In probing for sequences of other HCV subtypes, workers in different regions would have been expected to find different examples of HCV subtypes. There was no expectation that workers would find HCV subtype 1d sequences comprising the sequences identified in claim 64 instead of other sequences not listed. Although possible, the art

was too unpredictable to make finding such sequences identified in claim 64 obvious to succeed. Therefore, the rejection is believed to be overcome.

Point 10 is directed to a rejection of claims 70-72 under 35 U.S.C. §103(a) as being unpatentable over Qu et al. and Okamoto as applied to claims 63-69 and 73 above, further in view of Chien (WO 93/00365). Specifically, Qu et al. and Okamoto teach HCV subtype 1d sequences, and Chien teaches methods of recombinant expression of HCV polypeptides as well as vectors and host cells for use in the methods.

First, Okamoto may not properly be used in this rejection for the reasons discussed above. Second, HCV subtype 1d sequences reported by Qu et al. have been distinguished from the sequences of the present invention by the amendment of claim 63 given above. As a result, recombinant expression of HCV polypeptides by combination of the methods of Chien using the sequences of Qu et al. would not render obvious recombinant expression of HCV polypeptides as recited in claim 63. Therefore the rejection is believed to be overcome.

The Examiner is invited to contact the undersigned attorney at (713) 787-1438 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,

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